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EXAMINER

FERNANDEZ, SUSAN EMILY

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1651

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/771,283

Applicant(s)

MAHER ET AL.

Examiner

Susan E. Fernandez

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>5/26/05, 9/2/05</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The Declaration under 37 C.F.R. §1.132 filed on October 3, 2005, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 1-7 are pending and are examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite since it is not clear how the recited steps screen a plurality of drug candidate compounds against a target ion channel. For example, there is not step recited wherein the effect of the drug candidate on the target ion channel is detected. Thus, claims 1-7 are rejected under 35 U.S.C. 112, second paragraph.

Claims 4-6 are rendered indefinite by the phrase “an ion channel of interest” since it not clear whether “an ion channel of interest” is the “target ion channel” recited in claim 1.

Claim 7 is indefinite since the phrase “said one or more cells” lacks antecedent basis. It is not clear whether “said one or more cells” refer to the “host cells” recited in parent claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Catterall et al. (US 5,437,982).

Catterall et al. discloses a method of identifying specific inactivation gate inhibitors of a sodium channel. Example 1 describes the steps involved in this method, wherein the host cells, Chinese hamster ovary cells, are first transfected with wild-type Type IIA sodium channels, the target ion channels (column 13, lines 10-13). Additionally, mutant (F1489Q) sodium channels are also expressed in other host cells (human kidney carcinoma cells), and these mutant channels are also target ion channels. The effects of a drug candidate, the KIFMK gate peptide, is observed on these target ion channels by introducing the KIFMK gate peptide into the cells (column 13, lines 18-27), and then applying a series of 10 Hz voltage pulses which were applied at different voltages (column 13, lines 27-29). These voltage pulses are depolarizing and activate (open) the Type IIA sodium channels (column 5, lines 42-44). Therefore, instant claims 5 and 6 are anticipated by the reference. It is noted that the ion channel is cycled between different voltage dependent states (closed state to an open state, or closed state to an inactivated state), as the cell membrane of the Chinese hamster ovary cells are repetitively depolarized (column 6, lines 1-7). With respect to the inhibitory effect of KIFMK on sodium channels, the experiments demonstrated that, "...there is no appreciable block when the channels are not repetitively

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cycling between the closed, activated and inactivated states” (column 13, lines 59-62). Clearly, instant claim 4 is anticipated by Catterall et al. A holding of anticipation is clearly required.

Claim Rejections - 35 USC § 103

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Catterall et al. in view of Tung et al. (Biophysical Journal, 1992, 63(2): 371-386).

As discussed above, Catterall et al. anticipates claims 1, 2, and 4-6. However, Catterall et al. does not expressly disclose repetitive application of biphasic electric fields.

Tung et al. discloses comparison of the effects of biphasic and monophasic electric fields on the electrical stimulation of cardiac cells (abstract). It was noted that “strength-duration curves derived from field stimulation show that over a wide range of pulse durations, biphasic waveforms can recruit and activate membrane patches about as effectively as can monophasic waveforms having the same total pulse duration” (abstract).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to practice the screening method with biphasic electric fields instead of monophasic electric fields.

One of ordinary skill in the art would have been motivated to make this substitution in order to have stimulated the cells with a reasonable expectation of success. A holding of obviousness is clearly required.

Claims 1, 2, and 4-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Catterall et al. in view of Tsien et al. (WO 96/41166) or Denyer et al. (Drug Discovery Today, 1998, 3(7): 323-332).

As discussed above, Catterall et al. anticipates claims 1, 2, and 4-6. However, Catterall et al. does not expressly disclose a method wherein the host cells comprise a voltage sensor.

Tsien et al. discloses a screening method for identifying drugs that affect ion channel activity corresponding to changes in membrane potentials in cells (pages 42 and 43). The invention comprises the steps of loading the cells with first and second reagents for measuring membrane potential (page 42, lines 31-33). The first reagent comprises a transmembrane potential redistribution dye, also described as a hydrophobic fluorescent ion capable of redistribution upon changes in membrane potential (page 3, lines 7-11). Furthermore, the transmembrane potential redistribution dye is considered an ion sensitive fluorescent molecule and an electrochromic transmembrane potential dye. The second reagent comprises a chromophore, preferably a fluorophore capable of FRET or electron transfer (page 3, lines 25-30). Thus the second reagent is considered a FRET based voltage sensor, an electrochromic transmembrane potential dye, or an ion sensitive fluorescent molecule.

Denyer et al. reviews high throughput screening (HTS) methods for voltage-gated ion channel modulators. Radiotracers, including radioactive ions, are noted for their use in tracing ion flux through ion channels (page 328). Furthermore, high throughput methods have been established for enabling ion channel assays with radiotracers.

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At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have injected the host cells of the Catterall invention with the voltage sensors disclosed in Tsien et al. or the radiotracers disclosed in Denyer et al.

One of ordinary skill in the art would have been motivated to do this since the use of voltage sensors disclosed in Tsien et al. and Denyer et al. would served equivalently to the current measurements taught in Catterall et al. in measuring the effect of the drug candidate on the target ion channels. Thus, a holding of obviousness is clearly required.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.


Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1651

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PRIMARY EXAMINER